

which actuate a prisoner. And an investigation with negative results in such a case would be strong proof that the suspected mental state was within normal limits. To such uses the test may be constantly put.

A young girl was the object of much solicitude on the part of her parents, her physician, and her teacher. She was impulsive; did not care to study; defied her parents; on two occasions she marched out of school, vowing she would never come back. And one day, without a word to any one, she cut off all her hair. They all thought that some hidden delusion or some insane impulse alone could explain such behavior. The reaction words in the association test showed plainly the "schon erlebtes" of Ziehen—for example, the childish type of mind in which the associations aroused have to do with personal experiences, not abstract ideas. There was no lengthening of association time, except for a few recent and unimportant emotional complexes. There were no traces of sexual traumas, paranoid associations, or psychic points of origin of morbid impulses. The result of the test was, therefore, negative. And therein lay its value. For the negative findings excluded the probability of the existence of motives of insane character. And these negative findings were further entirely in accord with outside information in the case. The child was headstrong and self-willed, and had missed judicious parental supervision. But these facts by themselves were not sufficiently evident to have made it possible to regard the patient's peculiarities as within the limit of normal. With the association test such a diagnosis became almost certain.

THE IMPORTANCE OF BLOOD CULTURES IN THE STUDY OF INFECTIONS OF OTITIC ORIGIN.¹

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ALTHOUGH we made some studies of the bacteriology of the blood in cases of otitic infection some years ago, our interest in the subject was particularly aroused by a case in which the clinical diagnosis could not be definitely established, and in which the finding of streptococci in the blood led us to believe that it would be wise to explore the mastoid process, because the patient had a moderately

¹ Read at a meeting of the Association of American Physicians, Washington, D. C., May 11 and 12, 1909.

marked otitis media, and no other focus could be found from which the streptococcus might have entered the blood current. Not only was mastoid disease found, but there was also a sinus thrombosis present. A short time later a second case of the same type came under observation. We then decided to follow up the bacteriology of the blood more systematically in cases of acute and chronic ear disease, and encountered some other cases in which the bacteriological examinations were very valuable. In the last two years we have paid particular attention to this subject and will report in this paper a study of 163 blood cultures in 100 cases.² We have considered it advisable to present our results up to the present time for several reasons. In the first place, we believe that not sufficient attention has been paid by the internist to the border line work between otology and internal medicine. And it is the internist upon whom the responsibility often devolves of deciding whether an otological case should be operated upon or not. In the second place, the work illustrates very well how valuable a comparatively simple laboratory method may be in leading to important diagnostic and therapeutic conclusions. And thirdly, the studies, we believe, will be of interest because of the light they throw upon the question of the significance of certain forms of bacteremia.

We shall not discuss the literature to any great extent, partly because we wish to include it in a later larger publication, and partly because much of it is based on bacteriological methods, the results of which cannot be accurately compared to the results obtained by our present methods. One of us (Libman) has given a brief summary of our earlier results on some former occasions.³

As part of our study we investigated the bacteriology of otitis media (particularly the acute forms) to ascertain the relative frequency of the organisms most commonly involved in the causation of the disease. We studied 277 cases with particular reference to the occurrence of streptococci, *Streptococcus mucosus*, and the pneumococcus. The organisms that are next most commonly found are the staphylococci, *Bacillus pyocyaneus*, and *Bacillus proteus*. Mixed infections were not uncommonly found.⁴ We classified the streptococcus, *Streptococcus mucosus*, and the pneumococcus according to the classification that we have adopted as the result of studies made in our laboratory, particularly by Dr. Buerger⁵ and later by Dr. Rosenthal together with one of us (Libman⁶).

² The actual number of cases is somewhat smaller than this, as some of the cases are listed twice, because they were first admitted to the hospital for otitis media and mastoid disease and then discharged and later returned with a suspected sinus thrombosis.

³ Gruening, Libman, and Epstein, *Transactions of American Otological Society*, 1906; Libman, *Archives of Otology*, 1908, No. 1, p. 22.

⁴ For fuller details see Libman, *Archives of Otology*, 1908, viii, No. 1.

⁵ *Jour. Exper. Med.*, August 25, 1905, vol. xiii.

⁶ *Trans. New York Path. Soc.*, February, 1908. A full report of studies will be published in the near future.

In the 277 cases which we studied we found streptococci present alone or with other organisms in 189 cases (81.46 per cent.), *Streptococcus mucosus* twenty times (10.34 per cent.), the pneumococcus nineteen times (8.2 per cent.). The earlier authors found the pneumococcus present more frequently than the streptococcus, but the more recent writers (Leutert, Funke, Suepfle, Wittmanck, Mark) found the streptococcus present more frequently than the pneumococcus. It is to be noted that while *Streptococcus mucosus* is morphologically a streptococcus, it is more closely allied from a biological standpoint to the pneumococcus.

Notwithstanding the fact that the pneumococcus has been found frequently by many authorities in the middle ear, and notwithstanding the fact that we have found the organism in a certain number of cases, there are hardly any records of sinus thrombosis being due to the pneumococcus, and we have not met with any such cases. The few cases that are to be found in the literature are not definitely proved, because the methods used for identifying the organisms as pneumococci are not stated. It has been shown in our laboratory by Drs. Buerger and Ryttenberg⁷ that the pneumococcus can be so changed by its sojourn in the blood that it may be very difficult to differentiate it from the streptococcus. This fact must be taken into consideration, for it might occur that we might find an organism that looked like a streptococcus in the sinus and it might prove to be a changed pneumococcus. We have investigated this point, and have not had any such experience in our sinus thrombosis studies. It is necessary to study a large number of cases so as to determine definitely how frequently the pneumococcus causes a sinus thrombosis and whether the pneumococcus really causes a less serious local form of otitic disease than the streptococcus.

The literature concerning blood cultures in cases of otitic infection is very meagre. Besides the work of Kobrak, which we shall discuss directly, there are practically no systematic studies of the subject. A review of what has been done along this line up to 1907 is given by Hasslauer.⁸ The work of various investigators which is cited by Hasslauer cannot be used for comparison with our own work for the reason that so few cases were studied by each author, that the bacteriological methods varied very strikingly, and that hardly any of the authors made a comprehensive study of the primary focus, the blood in the general circulation, and the metastases. Some examined only the blood of the sinus. In general, one can

⁷ Jour. Infect. Dis., 1907, vol. iv.

⁸ Internationales Centralblatt f. Ohrenheilkunde, 1907, v, 1. See also Leutert, Archiv f. Ohrenheilkunde, lxxiv, 23. He gives references to a few further cases in which bacteriological examinations were made either of the sinus blood or of the blood of a peripheral vein. A case of general infection is mentioned briefly by Lenhartz (Septische Erkrankungen, 1903, p. 335), in which there was a remarkable decrease in the number of colonies of streptococci in the blood in a case of otitic infection with recovery. No data are given as to whether the patient had a sinus thrombosis or not, or whether any operations were performed.

draw the conclusion that the streptococcus was found in most of the cases.

Kobrak⁹ found streptococci predominating in the primary focus. He then studied 20 cases of acute otitis media, which were accompanied by fever in the first few days, believing that he would find that a bacteriemia was responsible for the fever. In all these cases the blood proved to be free from bacteria. He later took blood cultures only in cases of marked severity with fever of long duration, and he states that he found positive results only if the fever was pyemic, that is in so-called "septic cases." In 11 cases in which a positive blood culture was obtained, he found streptococci seven times, *Streptococcus mucosus* twice, the pneumococcus once, and the staphylococcus once. Of the 7 streptococcic cases, 4 died, all, as he states, "markedly septic." He states that in one case there was only a peribulbar abscess, and in another there was a direct infection from the ear. In the 2 mucosus cases the organism was also found in the cerebrospinal fluid.¹⁰ His total studies of streptococcic cases comprise 28, with general infection in 7. In 17 pneumococcic cases he found the pneumococcus in the blood once only.¹¹ He remarks that in cases of otogenic "sepsis" the decrease in the number of colonies in the blood and in their hemolytic power is of no significance, but rapid increase in the hemolytic power or in the number of colonies renders the prognosis very bad. The author does not give details as to the clinical course of these cases, nor the details of the post-mortem reports in the fatal cases. It can not be determined in how many cases it was possible that the patient had a sinus thrombosis from which he recovered without operation, nor can it be determined whether autopsies were performed in the fatal cases, and if so, how carefully the veins were examined.

Since we have paid closer attention to this subject we have made blood cultures in 50 cases of mastoid disease with recent or old otitis media, and in 10 cases of uncomplicated otitis media. Some of the cases of mastoid disease were accompanied by extradural abscesses. About one-half of the cases had at some time or other a temperature of 102.5° F. or over, some had a lower temperature, and some were practically afebrile. In a few of the cases the otitis media was bilateral. In our older series of cases we had positive results in two fatal cases of otitis media, but in both instances the blood cultures were taken but a short time before the fatal termination. In neither case is there a record of an accurate examination of the sinuses and the jugular bulbs.

⁹ Allg. med. Centralzeitung, 1907, lxxvi, 299. See also Verh. der Deutsch. Otol. Gesellsch., 1907, xv, 93.

¹⁰ As will be seen later, we have also had positive results in otitic meningitis due to *Streptococcus mucosus* and to the pneumococcus.

¹¹ He does not state how the pneumococcus was identified.

Our method, in brief, was to withdraw from 10 to 25 c.c. of blood from one of the arm veins (if necessary, from some other vein), and to incubate the material in agar, glucose agar, serum agar, glucose serum agar, and in bouillon and glucose bouillon with and without serum. If a large amount of blood was obtained, nearly all of these media were used. When a small amount was used, preference was given to the media containing glucose and serum. We often tested the value of using the blood in smaller and larger amounts in the various media. No differences were found. The plates and flasks were incubated for five days, subinoculations being made from the flasks (after shaking) in glucose bouillon and on serum glucose agar. In children we have often been compelled to use a smaller amount of blood, particularly in infants. We might state here that our studies in infants and young children are not yet extensive enough to warrant deductions.

Kobrak is not the only author who claims to have found a general infection in cases of otitis media without involvement of the sinuses or meninges. There are other scattered reports of such cases. It is essential to study a very large series of cases of uncomplicated otitis media and mastoiditis to determine the real frequency of such an occurrence.

Our positive results in otitis cases have been found only in those complicated by meningitis or sinus thrombosis (of course we include here thrombosis of the jugular bulb). In the meningitis cases we have found the pneumococcus and *Streptococcus mucosus* in the blood. In some of these cases a complete postmortem examination was not permitted, and we cannot state whether an infection of the veins was also present or not.

Before the cultures were made exclusively by one of us (Celler), we had a series of 14 cases in which the blood cultures were taken in different cases by different men, and in which repeated cultures were not made. Of these 14 cases, bacteria were found in 9, giving a percentage of 64. The later series comprises 16 cases, of which 14 gave positive results, giving a percentage of 87.5. In one negative case the clot obtained at the time of operation was found to be sterile; it was inoculated on media after being thoroughly ground up. In the other case we did not have the opportunity of seeing the clot, but the surgeon informs us that it was parietal and that it looked like an organizing non-purulent thrombus. It is possible that the high percentage of positive results is due to the fact that repeated cultures were made and that in a number of cases the cultures were made earlier than we were accustomed to make them a few years ago. If we reckon together both sets of cases, we have a total of 30 cases with 23 positive blood cultures (77 per cent.).

In the old series of cases streptococci were found in all of the 9 positive cases (during part of this time an accurate identifica-

tion of *Streptococcus mucosus* was not yet being made in the laboratory). In our second series streptococci were found eleven times, *Streptococcus mucosus* twice, and *Bacillus proteus* once. It will be noted, as stated before, that we have not found the pneumococcus in any of the cases. In our subsequent discussion we shall base our remarks only upon the cases in which the streptococcus and *Streptococcus mucosus* were found, classifying them for clinical purposes together.

In one positive case *Streptococcus mucosus* had been found in the primary otitis media and in the pus from the mastoid, but an ordinary streptococcus was isolated from the blood. The patient had been discharged from the hospital with an open wound, in good health, and returned later with a sinus thrombosis. The wound could have easily been secondarily infected by a streptococcus during the weeks that elapsed between the time of the mastoid operation and the time of development of the sinus affection. In cases in which there is a mixed infection of the middle ear, only one of the organisms may be found in the pus in the mastoid bone. In the case of general infection by *Bacillus proteus*, which we have cited above, the cultures from the middle ear also showed a large number of streptococci.

According to our recent experience, it would appear that nearly all cases of sinus thrombosis are accompanied by a bacteriemia at some time or other. We are inclined to believe, from a general survey of all our records,¹² that there may be early no bacteriemia, that the bacteria may then be found perhaps in increasing number, and that it is possible for the bacteria to decrease in number and even to disappear before there has been any operative interference.

It is of interest to attempt to explain the occurrence of the negative results in some of the cases. Different explanations probably hold for different cases. In some cases (probably rarely) the clot is sterile and it is easy to explain the absence of bacteria in the blood. In some cases the blood culture may have been taken before the bacteriemia had been established or after the bacteria had disappeared from the blood. Bacteria may be present in the blood in too small number to be found in the amount of blood used in making the cultures. This would not necessarily mean that there had not been many bacteria discharged into the jugular vein, because there is a possibility that large numbers of the bacteria may be rapidly killed off, in which event few or none might be found in the blood obtained from one of the peripheral veins.¹³

It is also possible that in certain cases there is below the infected clot an obturating, non-infected clot which prevents the bacteria

¹² It is difficult to draw conclusions from any one case, because cultures cannot be taken frequently enough to make thorough observations.

¹³ See Leutert, *infra*.

from entering the circulation. One can also imagine the possibility of there being an infected clot which completely closes the vessel. Another possible explanation is that, in the course of the infection the blood may acquire a higher bactericidal power.

In some instances a bacteriemia is cut short by tying the jugular vein. In such cases metastases may develop even though the blood is free from bacteria. They may develop from bacteria or bits of clot deposited in various parts of the body before the vein has been ligated. All such foci need not appear at once. We must also remember that at the time of operation, particularly if the sinus itself is exposed before the jugular vein is tied, and there is a thrombosis present, bits of infected clot may be scattered. In this way also metastatic foci could develop without a persisting bacteriemia.

In some cases in which the jugular vein has not been tied, metastatic abscesses may be found in the lungs and there may be no bacteria in the circulation. In these cases, which are generally older ones, we are often dealing with a softened clot from which pieces are broken off which contain bacteria which set up secondary foci. The probable explanation is that free bacteria are promptly killed off, but that those carried in pieces of thrombi are protected during their passage through the blood from the bactericidal power of the latter. In our experience, the metastatic foci in cases of so-called "pyemia" do not cause a bacteriemia.

Our studies show that cases in which streptococci are found in the blood after the disease of the mastoid is properly operated upon, and in which clinical symptoms persist and no other cause can be found for a streptococcemia, are cases of sinus thrombosis. It is very important to consider carefully the possibility of other causes of streptococcemia (or other bacteriemia) in such cases. In our investigations the cases of otitic disease which even before operation showed a streptococcemia, and in which other causes for a streptococcemia could be excluded, showed sinus thrombosis at operation or at autopsy. We would not be willing to state absolutely, however, that in all the cases in the latter group a sinus thrombosis would be found, because our studies in cases of acute otitis media and mastoiditis uncomplicated by sinus thrombosis are not yet extensive enough. But if the middle ear has been properly drained and the mastoid has been operated upon and there is no meningitis present and no other cause found to explain the persisting bacteriemia and persistent clinical symptoms, we come, practically by exclusion, to the assumption that a lesion is present in the veins which causes the bacteriemia.

It is necessary, in studying such cases, to take a number of points into consideration. There is always a possibility that a patient is suffering from a general infection in the course of which he develops otitis media or mastoid disease. This is particularly liable to occur in cases of general pneumococcic or streptococcic infection, cases of

pneumonia,¹⁴ and cases of typhoid fever. In cases of typhoid fever it is essential to know whether or not the otitis media developed after the patient had already had fever. The presence of typhoid bacilli in the blood, if one were in doubt as to whether marked symptoms were due to an otitis media by itself or to a complicating typhoid, would make us feel that we could ascribe the fever to the typhoid infection alone. The rest of the diagnosis would have to be based on clinical signs and on the development, possibly, of a streptococcemia, although it is to be remembered that rarely a patient with typhoid fever suffers from mixed infection with streptococci. In some of these cases it might be very difficult to come to a conclusion as to the exact condition in the mastoid and surrounding parts.

It is also important to note the possibility of a bacteriemia following operative interference upon the middle ear or the mastoid process. In all of our cases in which we found streptococci in the blood after the mastoid had been operated upon, a sinus thrombosis was found. But from our experience with postoperative bacteriemia after operations in other parts of the body, we believe that one should be very careful in judging of positive blood cultures if the blood cultures are taken directly after there has been operative interference.

It has often been pointed out that difficulties might arise because of the possibility of a developing erysipelas or the presence of an angina. It has been feared that one would have difficulty in interpreting a streptococcemia in a case of otitic disease if either of these conditions were present. As a matter of fact, in our experience we have very rarely found streptococci in the blood in erysipelas, and then it has only been in fatal cases. This experience seems to be shared by other investigators of the blood in this disease.

The question of a possible confusion because of the presence of an acute angina is a very important one. Streptococcemia in such cases is very infrequent. In our experience we have fortunately had no trouble from this source.

Leutert¹⁵ and, later, his assistant, Nuerenberg,¹⁶ have suggested a method for attempting to overcome the difficulty involved under the conditions mentioned above. Leutert has suggested taking blood cultures from the sinus and from the jugular vein and an arm vein. He believed that if more streptococci were found in the blood of the sinus than in the blood of the jugular vein or an arm vein, or if organisms were found in the blood of the sinus and none in the blood of the peripheral vein, one could conclude that the bacteria were gaining entrance to the circulation from the sinus, and that the bacteria were not entering the blood from the coincidental angina

¹⁴ If in a case of otitis media due to streptococci, pneumococci should be found in the blood, one would have to think of a developing lobar pneumonia.

¹⁵ Archiv f. Ohren., lxxiv, 18.

¹⁶ Münch. med. Woch., No. 51, p. 5227.

or erysipelas. They describe several cases in which they found this method valuable, but they admit what at once must strike any one as a serious objection. The results cannot always be depended upon, because the sinus is aspirated through an infected area. In one case we aspirated the sinus because we could not obtain blood from one of the peripheral veins. The blood from the sinus was sterile; a clot found at operation was also sterile.

In our cases the number of bacteria found in the blood in cases of sinus thrombosis accompanied by bacteriemia has varied from less than one to the cubic centimeter up to 245 to the cubic centimeter. In all of the cases, except those that died within a few days after admission, we attempted to ascertain how rapidly the bacteria disappeared from the blood after operative interference. In all except three cases, which we will describe later, the bacteria disappeared rather promptly. As a rule, the bacteria did not disappear until the jugular vein was tied. There were two cases, however, in which the bacteriemia disappeared after a clot was removed from the lateral sinus and the jugular vein was not tied.

In our early studies we took the secondary cultures forty-eight to seventy-two hours after operation, and we found that the bacteria had disappeared in all the cases except in the three soon to be described. In some of the later cases we took the blood cultures twenty-four hours after ligation of the jugular vein, and these cultures also gave a negative result. It is very remarkable to see as many as 245 streptococci to the cubic centimeter of blood disappear within twenty-four to forty-eight hours after ligation of the jugular vein. In one case there were seven colonies of streptococci to the cubic centimeter of blood; within eight hours after ligation of the jugular vein the blood culture was negative and remained so.

The three cases in which bacteria did not disappear promptly after ligation of the jugular vein were of particular interest. In one the streptococcus persisted in the blood after the clot had been removed from the lateral sinus and the jugular vein had been tied.¹⁷ The bulb of the jugular vein was then exposed, a clot removed, and then the bulb packed; the bacteriemia (there were two colonies to the cubic centimeter of blood) then promptly disappeared in less than four hours. In this case we believe the continuance of the bacteriemia was probably due to infection of the general system by way of the inferior petrosal sinus.¹⁸

In another case the bacteriemia disappeared after ligation of the jugular vein, but a couple of metastatic deposits developed.

¹⁷ In all these cases in which the jugular vein was tied a section of the vein was resected. The operation on the sinus usually consisted of removing as much clot as possible, and packing.

¹⁸ We shall attempt to continue the study of the rapidity of the disappearance of organisms from the blood of these cases by making cultures at still shorter intervals after operation than we have heretofore done. We shall report any results that we may obtain at a later time.

The patient also had a right-sided mastoiditis, which was operated upon. Later, streptococci were again found in the blood, the patient developed more metastases, and finally recovered. Although at the time we did not think of the possibility, we now believe that it is probable that in this case there was also a thrombosis on the right side, from which the patient recovered without operation. We know that some cases of sinus thrombosis with or without metastases have recovered without operation. The same holds true of infected veins in other parts of the body.

In a third case in which the bacteria persisted even after the local focus had been thoroughly dealt with (and this was confirmed at autopsy), the persistence of the bacteriemia was due to the development of an acute (ulcerative) endocarditis.

The studies on the disappearance of the bacteria in these cases have almost the value of experiments. They show that the bacteriemia is due to discharge from the local focus, and that the bacteria remain in the blood after the local focus has been thoroughly dealt with (when that is possible) only if multiplication of bacteria occurs in the blood or if an acute endocarditis is established. Both these conditions have been very unusual in our experience.¹⁹

What then, according to our experience, is the value of blood culture studies in cases of otitic infection? We will discuss first the significance of positive results and then briefly the value of negative results:

1. SIGNIFICANCE OF POSITIVE RESULTS. (A) A positive blood culture is valuable when there is doubt as to the existence of a sinus thrombosis after a patient has been operated upon for mastoid disease. In many cases the diagnosis is clear enough clinically, but in a certain number of cases in which the mastoid disease had been thoroughly dealt with, and in which there were clinical symptoms still present, and in which the otologist was not sure that there was still further local disease, the finding of streptococci in the blood has given the indication to explore the sinus, and in all the cases of this type a sinus thrombosis was found. As we have stated before, it is essential to exclude all other causes of streptococcemia.

A case worthy of citation here is that of a man, aged thirty-three years, who developed pain in the left ear, following an attack of grippe, four weeks before admission to the hospital. There was increasing tenderness over the mastoid process and slight fever, but at no time any ear discharge. The drum membrane was slightly reddened. It was also noted that there were very tender and large lymph nodes behind the angle of the jaw. During the first three days of the

¹⁹ In the case of general infection by *Bacillus proteus*, which is mentioned earlier in the paper, the bacilli also persisted until death, but in this case the local focus could not be thoroughly dealt with, because the thrombosis had extended into both petrosal sinuses on the same side, both cavernous sinuses, and into the lateral sinus of the opposite side.

patient's stay in the hospital his temperature ranged between 100° and 102° F., the pulse rate varying from 70 to 84. On April 20 the temperature rose to 103° and he was operated upon. A chronic mastoiditis was found. After the operation the temperature dropped, so that on April 24 and 25 it was practically normal. On April 26 there was a slight chill and rise of temperature to 102° F. During the following four days the temperature was about 101° F., once reaching 103°. On April 29 the patient was allowed to be out of bed. The pulse rate was 72 to 80. The leukocyte count was 21,200, the differential count showing 80 per cent. of polymorphonuclears. In the early afternoon of May 2 a blood culture was made, the patient being up out of bed in a chair. On the evening of the same day the patient had a chill; his temperature rose to 104.6°. The following day, when the temperature was down to 100°, we reported that there were 210 colonies of *Streptococcus mucosus* to the cubic centimeter of blood. As there was no other cause for such an infection, it was decided to operate again, in the expectation of finding a sinus thrombosis. The operation was performed the same afternoon. A thrombus was found in the lateral sinus. The jugular vein was ligated in two places, the intervening part being removed. On the following day, May 4, the blood culture was found to be negative. The temperature was normal by May 6. In this case the clinical symptoms which suggested making the blood culture were the moderate irregular fever, the increase in the leukocyte count, postmastoid tenderness, and a rather sickish look of the patient.

Another very striking case was that of a girl (M. L.²⁰), aged twenty-two years, who was admitted to the hospital on January 28, 1908. The patient at first suffered from la grippe, followed by spontaneous perforation of the left drum membrane with purulent discharge. Four days before admission the right drum membrane was incised; this was followed by discharge. The temperature at the time ranged between 99° and 100°. On the day before admission the temperature rose to 103°, the patient complaining of marked deafness. There was pronounced nystagmus, some nausea and vomiting, and considerable frontal headache. On January 28 and 29 the temperature was between 101° and 102°. On January 30 the temperature was 103°; pulse, 90 to 104. On the same day operation was performed on the left mastoid. Pus was found in the cells of the tip of the mastoid, in the antrum, and over the sinus; the sinus itself appeared normal. On January 31 the temperature dropped to 101°. On February 1 it rose to 104°.

On the same day operation was performed for acute mastoiditis on the right side. There was found moderate-necrosis of the cortex and of the tip. Some pus was found in the antrum. On February 2 the temperature was 103°. On February 3 the temperature rose

²⁰ This and the previous case occurred in the private practice of Dr. Seymour Oppenheimer.

to 104.4°. A blood culture was made, and three and one-half colonies of streptococci to the cubic centimeter of blood were found. On the following day, when the report was handed in, the temperature was 100.8°. On February 5 another blood culture was taken at a time when the temperature was 103°, and we found fifteen colonies of streptococci to the cubic centimeter of blood. We advised exploratory operation for sinus thrombosis.

But during the next week the patient appeared to be doing so well, the temperature not rising above 103°, as a rule, that the otologist did not consider that he was warranted in operating any farther on the patient for the time being. On February 13, at a time when the patient had a temperature of 103.4°, another blood culture was taken, and there were found to be present sixty colonies of streptococci to the cubic centimeter of blood. On the following day, when the report was handed in, the temperature was only 101°, and operative interference was again deferred. On February 15 the temperature rose to 103°, and on the 16th it dropped almost to 99°. A blood culture was taken on that day at 4 P.M., the temperature being 99.6°, and again there were found to be sixty colonies of streptococci to the cubic centimeter of blood. For the next two days the temperature did not rise above 100.4°, and the patient seemed to be doing remarkably well. On the morning of February 19 the temperature was 99°. At noon the temperature was 100°; in the afternoon the temperature began to rise.

On examination of the patient there was found to be tenderness in the region of the jugular bulb, and there were some enlarged tender lymph nodes along the course of the jugular vein. A blood culture taken at this time, 3.30 P.M., showed two colonies of streptococci to the cubic centimeter of blood. At 4 P.M., when the temperature was about 102.5°, the patient was operated upon. The jugular vein was exposed in the neck and part of it resected. About one-half inch above the entrance of the facial vein the wall of the jugular vein was white in appearance, very firm, and the vein appeared to be flattened. There was marked inflammation of the lymph nodes about the vein. A non-suppurative clot was found in the vein which closed the vessel as far down as the point of ligation and extended slightly on the wall of the vein for a short distance below the upper ligature. The temperature the same night rose to 103°, but dropped the next day to 99°, and never rose above 99.8° after that, the patient making a complete recovery. A blood culture made on February 22, three days after ligation of the jugular vein, proved to be negative.

This case is one of the most remarkable in the entire series which we have studied. The suspicion of a sinus thrombosis was aroused by the blood culture results over two weeks before it was clinically considered proper to operate for supposed sinus thrombosis. It is interesting to note that the streptococci gradually increased in

number, and then decreased even before the jugular vein was tied. If the jugular vein had not been tied at the time it was, we believe it is possible that the blood cultures might have become negative before the ligation was performed. There are a number of other points of interest about this case, especially in regard to the leukocyte counts, a discussion of which we must postpone for another time.

(B) In certain cases, after the sinus has been explored and a clot has been removed and the jugular vein has not been ligated, the persistence of streptococci in the blood has given the indication to tie the jugular vein, and, as we have previously stated, in almost all of the cases the bacteria then promptly disappeared from the blood. A case showing in a striking manner the value of such a finding will be given in the case (Levin) to be described under the next heading.

It should be noted here that while the bacteria usually promptly disappeared after ligation of the jugular vein, the clinical symptoms (particularly the fever) do not always as promptly abate. In some cases the patient will still have fever, due possibly to local conditions in the wounds, or due to metastases previously developed or being developed, or due to some other intracerebral complication or to some intercurrent disease.

We have already pointed out that in one case the bacteria did not disappear even after the jugular vein was ligated, but did disappear after the jugular vein was exposed, a clot removed, and the vessel packed. This case (Klein) will be described briefly under the next heading.

(C) The most valuable field for the blood culture studies has been in the border line cases, in which it would have been very difficult to come to a definite conclusion without the use of the cultures. The first case of this type, a male, aged seventeen years, was admitted to the hospital in the service of Dr. Rudisch on January 3, 1904. For the first three days after admission he had an almost constant temperature of 103° to 105° . For the following three days the temperature ranged between 100.5° and 103° , the pulse rate varying from 92 to 100. The history given was that the boy had suffered from headache and malaise for eight days. He had then become feverish and chilly and remained in bed. He had then developed abdominal pain for one day. Three or four days before admission he had severe shaking chills followed by sweating. The boy was sent into the hospital for supposed typhoid fever. On examination by one of us (Libman) on the day of admission the boy did not give the impression of suffering from typhoid fever. There were no rose spots present. There was no enlargement of the spleen. On thoroughly examining him it was found that he had a moderately marked otitis media on the left side.

The otologist was then called in to see the patient; he punctured the left drum, and a little seropus was evacuated. The leukocytes

numbered 17,600. There was some tenderness over the tip of the mastoid. The otologist did not believe that the otitis media by itself could explain the clinical picture. The Widal examination proved to be negative. It was then suggested that a blood culture be made so as to determine whether any organisms were present in the blood. It was thought that if typhoid bacilli were present in the blood the case would be regarded rather as one of typhoid fever with a complicating otitis media, but if streptococci were found in the blood it would be proper to advise operation upon the mastoid, because there was no other demonstrable focus found from which the organisms might be entering the blood current. At this time we believed that more extensive trouble might be found than there appeared to be according to the local findings. On January 4 the blood culture was taken, and on January 5 it was reported that streptococci were in the blood. The mastoid region was explored on the same day by Dr. Gruening. Not only was mastoiditis found, but there was a clot in the lateral sinus which extended down as far as the exposure would allow. A perisinuous abscess was also found. The patient's condition became so poor that the jugular vein could not be tied off. The temperature dropped next day to 100°, but during the next two days rose again to 102°. A blood culture was again taken on January 6, and streptococci were again found. At that time we did not understand the significance of the persisting bacteriemia, and did not urge further operation, but on January 8 Dr. Gruening, because of the persistence of the clinical symptoms, considered it advisable to tie the jugular vein. A blood culture taken on January 12 proved to be negative, as was also one taken on January 19. The patient developed a few metastatic abscesses which we believed were probably to be explained by the dissemination of bits of clot before the jugular vein was tied.

After the diagnosis in this case had been cleared up a history was obtained by careful cross-questioning of the patient and his relatives, which differed from that obtained on the admission of the patient to the hospital. Eight days before admission the patient had developed pain in the left ear. This pain lasted for three days. It was slight in the morning and moderately severe in the evening. The pain then disappeared, and the patient suffered from headache, which was first located in the left side of the head and then was frontal in character. He then developed abdominal pain.

We have previously in this paper drawn attention to the difficulties that might arise at times in the differential diagnosis between sinus thrombosis and typhoid fever. The complete question of differentiation, including the question of the clinical phenomena, we hope to take up on another occasion.

Shortly after seeing the case which we have just described, on January 21, 1904, a female patient, aged twenty-seven years, was admitted. The history given was that she was sick for fifteen days

suffering from severe occipital headache with stiffness and tenderness of the neck. She had had chills and fever coming on every second day and followed by profuse sweats. On examination of the patient perforations were found in both drum membranes. On the left side there was fairly marked tenderness behind the mastoid process and along the occipital ridge. There was no tenderness on the right side. There was no rigidity of the neck. On January 21 the patient had a chill and temperature of 105°. On January 22 the temperature was down to 102.4°; the leukocyte count was 13,000. On January 23 there was a chill in the early morning and a rise of temperature to 105°; the leukocyte count was 10,000. The spleen was palpable one finger below the free border; it was very firm. The otologist did not believe that in this case there was sufficient evidence of local trouble to warrant operation. The clinician in charge of the case was inclined to believe that the patient was suffering from malaria, but plasmodia could not be found.

We suggested that, before waiting for the result of treatment by quinine, it would be advisable to take a culture, which was accordingly done on January 23. On January 24 it was reported that there were streptococci in the blood. It was considered warrantable to explore the mastoid process, as there was a certain amount of suspicion from the local examination that there was more trouble there than the old otitis media, and because there was no other focus found from which the streptococci were gaining access to the blood current. The cortex of the mastoid was found thick and hard. In the antrum there was granulation tissue. The lateral sinus was found to contain a clot, part of which was decolorized. The clot extended around to the torcular. On January 25 the temperature was 98.8°. On January 26 the temperature was 102.8°. The margins of the wound were found to be necrotic. On the same day a blood culture was taken, which was found to be negative. The patient's temperature was normal by January 31, and she was discharged practically well on February 26. No metastases developed in this case.

A third illustrative case we will cite briefly: This patient was admitted to the hospital on February 28, 1909. He was a male, aged nineteen years, who had had pain in the left ear ten days before admission to the hospital; there was also profuse discharge. The following day the patient developed the same symptoms on the right side. At the time of admission to the hospital there was no discharge from the left ear, but the right ear continued to discharge pus and there was tenderness at the tip of the mastoid process. The patient stated that he had had several chills. On examination it was found that the drum membrane was reddened and there was a medium-sized perforation. There was tenderness over the tip of the mastoid process and slight tenderness in the region of

the jugular bulb.²¹ The temperature was irregular from February 28 to March 1, reaching 103° and 104°, and on March 2 only reaching 101.4°. It was not believed by the otologist that there was sufficient evidence of local trouble to warrant operation. The examination of the patient otherwise was negative, and a blood culture taken on March 2 showed streptococci, there being seven colonies of streptococci to each cubic centimeter of blood. The patient was operated upon on March 3. Just before the operation streptococci were again found in the blood, there being nine colonies to the cubic centimeter. At the operation the mastoid cells were found only slightly diseased. The wall of the sinus was thickened. A large amount of white thrombus was scraped out of the sinus. Free bleeding was established from the cerebral end of the sinus, but only a moderate amount of bleeding occurred from below. The patient was in too poor condition to tie the jugular vein. A blood culture taken a few hours after operation showed 165 colonies of streptococci to the cubic centimeter of blood (in this case the postoperative increase can be fairly ascribed to the operative interference). The following morning the blood culture showed less than one colony of the streptococcus to the cubic centimeter of blood. On March 5 it was decided, because of the persistence of streptococci in the blood and the continuance of clinical symptoms, to tie the jugular vein, which was accordingly done. A drain was passed down into the bulb of the jugular vein from above. The following day there were still streptococci in the blood, 200 colonies to the cubic centimeter, and streptococci persisted in the blood until the patient died. At the autopsy no further trouble was found in the sinus or in the jugular vein, but an ulcerative endocarditis was present.

In some cases it is very difficult to come to a conclusion unless one judges carefully all the facts. We have had two cases in which the conditions were particularly complicated. Unfortunately, both patients arrived at the hospital in very bad condition, and died within a few days.

The first case was a female, aged seventeen years. She gave a history of fever and headache lasting for two weeks, being accompanied by severe dry cough. On the afternoon of admission the right ear began to discharge. On examination there was found profuse purulent discharge from the right ear. There was tenderness over the tip of the mastoid and some tenderness along the jugular vein. The examination of the fundi showed some dilatation of the veins on both sides, more marked on the right side. The leukocyte count was 14,200; polynuclears, 76 per cent. The temperature on admission was 105°. On examining the lungs, crepitant

²¹ In a subsequent communication by one of us (Libman), dealing with a method for testing patients for their sensitiveness to pain, it will be shown that much stress cannot be laid on tenderness in the region of the jugular bulb unless the patient is normally hyposensitive.

rales were found at both bases. At the left base there was dulness, and on auscultation numerous rales and a rather large area of bronchial breathing. In this case the ear surgeon was not ready to operate because of the presence of the pulmonary phenomena, particularly on the left side. It was decided to wait before exploring the mastoid process until the blood culture was made. If pneumococci were found, it was decided that they might be considered an accompaniment of the lung condition. But if streptococci were found, it was considered that it would be justifiable to explore the mastoid region, as it was possible that they were gaining their entrance from that point, and the lung lesion might be secondary. The blood culture was taken on the day of admission at 7.30 P.M., and the following morning streptococci were found (one colony to the cubic centimeter). The mastoid process on the right side was explored. Granulations and pus were found. Pus was found in the lateral sinus. The jugular vein was then ligated. The patient died the following morning. A postmortem examination was not permitted.

The other case was that of a man,²² who was admitted to the hospital January 30, 1907. The patient had suffered for a number of days from a severe inflammation of the alveolar border of the right lower jaw, with an enlargement of the submaxillary lymph nodes. A few days later he developed pain in the right ear. A puncture was made, but no pus was found. A few days later there was a discharge of pus. The patient had high temperatures for several days before admission. There was tenderness and swelling of the muscles of the right calf, and the skin over them was reddened. There was but little mastoid tenderness. The patient was evidently severely sick and it appeared that the trouble in the right calf was a developing metastatic abscess. There was also some pain and redness of the first joint of the left thumb.

The question arose as to whether the metastatic abscess was due to infection of the sinus or to the infection of the lower jaw. We argued that in this case the presence of streptococci in the blood would suggest an exploration of the sinus, because in our experience the infections of the lower jaw, particularly those at the alveolar border, do not give a bacteriemia, and because one does not generally find secondary foci in such cases. Further, we knew that infections of the sinus were apt to be accompanied by a bacteriemia and that in some cases of otitic infection there was a tendency for metastatic processes to be established in the muscles.

The otologist decided in this case not to take any chances by waiting because the patient was so severely sick, and the patient was operated upon on the day of admission, a blood culture being taken just before the operation. At the operation a purulent clot was found in the lateral sinus and a clot in the upper part of the

²² This case was studied through the courtesy of Dr. Carl Kaller.

jugular vein. The jugular vein was resected. Streptococci were found in the blood (two and one-half colonies to the cubic centimeter). Streptococci were again found in the blood a few days later (three colonies to the cubic centimeter). The patient died a few days later; postmortem examination was not permitted.

These cases show clearly in what manner we have attempted to utilize the positive results in helping to diagnosticate doubtful cases. As we have already pointed out, it would seem from our studies that the streptococci remain in the blood in the cases of sinus thrombosis either because there is still trouble present in the veins or because endocarditis has been established. The establishment of endocarditis in these cases occurs, according to our experience, very infrequently. Multiplication of streptococci as a possible cause of persistence of streptococci in the blood, after proper attention has been paid to the local focus, must also be reckoned with as a cause of persistent bacteriemia. We have not found any instance of this occurrence in the series of cases upon which our report is based.

2. SIGNIFICANCE OF NEGATIVE BLOOD CULTURES. (A) We have shown that negative results can be obtained, even though not frequently, in cases in which a sinus thrombosis is present. The absence of bacteria in a doubtful case would make one hesitate in exploring for a thrombus until the possibility of all intercurrent diseases had been excluded, or until the symptoms had become so severe as to justify an exploratory procedure.

(B) If the blood culture should be negative and the symptoms should persist in a given case, whether there is a sinus thrombosis or not, acute endocarditis can be excluded. In such cases it is advisable to take two blood cultures. In our experience in cases of acute endocarditis due to ordinary streptococci (and staphylococci) bacteria are always found in the blood if two cultures are made.

(C) As we have already stated several times, if there has been a sinus thrombosis and bacteria have been present in the blood, and the jugular vein has been tied, a negative culture is of value in showing that the general invasion has been stopped.

(D) Occasionally a negative blood culture has been of value in cases with a clinical picture of rheumatism. It is very valuable in such cases to know that we are not dealing with an arthritis due to a general invasion by the ordinary bacteria.

The data which we have given are sufficient to show the great value of the investigation by means of blood cultures in cases of otitic infection. It is important to know that in no line of work are routine rules more disadvantageous in attempting to draw conclusions. Each case must be made the subject of a careful clinical and bacteriological study. We hope that our work will stimulate others, who are in possession of larger material, to investigate their cases according to the methods which we have suggested.

Most of the cases which form the basis of this paper occurred in the service of Dr. E. Gruening, to whose kind coöperation we owe the possibility of having made our studies. The recent cases were investigated through the kindness of Dr. F. Whiting. We are also much indebted to Dr. S. Oppenheimer for the privilege of making studies in a number of his cases and for the use of the clinical histories.

ADDENDUM.—Since reading this paper we have made cultures in 17 additional cases of otitis media and mastoid disease. In only 1 case were streptococci found in the blood, and in this case at operation a purulent thrombus was found in the lateral sinus. The streptococci disappeared from the blood within seven hours after operation. We have therefore now had 75 cases of otitis media or mastoid disease without sinus thrombosis or meningitis, and in all these cases the blood has been sterile.

Drs. A. Duel and J. Wright,²² of New York, reported a series of blood cultures made in cases of otitic disease, in which they obtained positive results in cases of uncomplicated otitis media and mastoid disease. The method used in the study of these cases was somewhat different from our own, inasmuch as the authors in most of their cases made a practice of incubating 10 c.c. of blood in flasks containing 150 c.c. of bouillon or glucose bouillon; after two to three days 15 to 30 c.c. of the contents of the flask was centrifuged and cultures were made on solid media from the sediment. Before reading the paper, Drs. Duel and Wright were kind enough to inform us of the method which they were using in the study of their cases, and since that time we have employed it in 11 cases of otitis media and mastoid disease, comparing it with our own method. The results were identical, all the cultures being negative. Besides this we made a study of 65 cases of local infections in different parts of the body of a type which, according to our experience, is unaccompanied by a bacteriemia, using both the strong concentration of the blood, as suggested by Dr. Wright, and also employing our own method. In all these cases the blood cultures were negative.

²² At a meeting of the American Otological Society held in Boston, June 1, 1909.